special construction and a well-cushioned, triangular pad, so as to exert required pressure upon the sacrum. Pressure on the upper or lower portion of the sacrum is regulated by means of two hard-tempered semicircular springs, to which webbing straps firmly attached are buckled in front. The pressure may be centred upon the upper region of the sacrum by drawing the upper straps tight while the lower ones are allowed to remain moderately loose, and *vice versa;* pressure may be made upon the lower region of the sacrum by drawing the lower straps tight. When required the apparatus may be retained in position by perineal straps, but when it is well fitted these are not necessary.

The principle sought for in any or all such appliances is the exertion of pressure upon the sacrum, either at its upper or lower part, according to the indications in the individual case.

Where deformity has existed for a long time it may become necessary to apply traction while the patient is in bed for a varying period before employing these appliances, while in some cases it is essential to fix the trunk and lower extremity until the subsidence of the active inflammatory symptoms.

3. *The after treatment,* which is often neglected, consists in developing the affected region by means of exercises, massage, vibration, and the application of the electric current to all the ligaments and fibrous structures around the articulation, so as to prevent future displacements. These *séances* should be prolonged and should be administered over long periods of time, in order to obtain the best possible effects from this line of treatment. Should any disease of the female genital organs be associated with displacements of the sacrum it is unnecessary to remark that the former class of affections should at once engage the attention of the gynecologist. In certain cases where non-operative measures have failed to give encouraging results, I contemplate some radical surgical operations, as plating the pubic bones and wiring the sacro-iliac articulation.

HEMOLYSIS IN VIVO AND IN VITRO AS DIAGNOSTIC OF CANCER.

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This work was undertaken for the purpose of comparing the skin reaction for carcinoma described by Elsberg, Neuhof, and

Geist,[1] with the hemolytic power *in vitro* of the serum of cancer patients, and to study the relation, if any, existing between these phenomena and the normal isohemolysins and isoagglutinins.

A number of observers have sought for some specific or diagnostic character of the serum of cancer patients. With this idea in mind, Crile[2] reported having found a marked hemolyzing power on the part of the serum of cancer patients, when allowed to act upon red blood cells of a normal individual. This he found in a surprisingly large number of early cases, although he stated that the reaction disappeared when the disease became advanced. Crile's work has not been generally confirmed. Other investigators have found cancer sera to possess hemolyzing power, but in a far smaller percentage of cases than Crile did. No one has been able to prove definitely the presence of a specific diagnostic substance in cancer serum. As to specific hemolysis, further study has shown the existence of isohemolysins in normal individuals and in a variety of diseased conditions. The hemolytic test of a serum *in vitro*, therefore, is considered of no great value from the clinical standpoint. Krida[3] has collected from the literature a total of 1812 observations by ten different workers on the hemolysins of cancer serum tested *in vitro*. Four hundred and seventy-two cases were carcinoma. Of these, 317 (67 per cent.) gave positive hemolytic tests, and 79 were benign tumors, of which 1 (1.25 per cent.) was positive. Five hundred and seven observations were made in a variety of diseases of which 74 (15 per cent.) gave a positive reaction. Five hundred and nine observations were made on normal individuals, of which 14 (2.6 per cent.) were positive.

Both the work of Moss[4] and our own investigations emphasize the inconstancy of the occurrence of hemolytic properties in the serum of carcinomatous patients when tested outside the body. They demonstrate, further, the not infrequent hemolytic power in the serum of normal individuals, and as well, in the serum of patients suffering from diseases other than cancer.

Weil[5] has studied the hemolytic action of extracts of normal organ and of tumor on normal red blood cells. He finds that extracts of necrotic tumors and of autolized organs possess much more hemolytic power than extracts of normal organs and of non-necrotic tumors. The hemolysin in the former is dialyzable and not inhibited by the action of serum, while that of the latter is non-dialyzable and serum inhibits its action. On this basis he seeks to explain the anemia and cachexia of malignant disease, suggesting that it is due to the destructive action on the red blood cells of substances liberated by the necrotic tumors.

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[1] Amer. Jour. Med. Sci., February, 1910.

[2] Jour. Amer. Med. Assoc., June, 1908, No. 23, l, 1883; Ibid., December, 1908, No. 24, li, 2030.

[3] Albany Med. Ann., No. 5, xxxi, 259.

[4] Johns Hopkins Bulletin, March, 1910, xxi, No. 228.

[5] Jour. Med. Research, 1907, p. 287; Ibid., 1908, xix, 281; Jour. Amer. Med. Assoc., 1908, li, 158; Jour. Med. Research, 1910, xxiii, 85.

The resistance of the red blood corpuscles to varying percentages of hypotonic salt solution has been studied in many conditions. It has been shown that in secondary anemias there is an increased resistance of the red cells.

The idea of testing the resistance of normal red cells in cases of carcinoma, by subcutaneous injection of the washed cells was suggested by Elsberg, Neuhof, and Geist.[6]

Krida[7] repeated the work of Elsberg, Neuhof, and Geist, and reported a series of 76 tests. Of 12 cases of carcinoma the reaction was positive in 9 (75 per cent.). He does not separate the cases into early and advanced carcinoma, as do Elsberg, Neuhof, and Geist. He justly raises the question as to whether this line is to be drawn. He did not find the reaction consistently absent in miliary carcinoma, as did the above observers. Krida states that if all their cancer cases are considered together, making 80 in all, the percentage of positive results would be about 77 per cent., a figure approximately identical with his own.

Risley[8] has also repeated the test in 100 cases at the Massachusetts General Hospital. The reaction was positive in 9 cases (33⅓ per cent.) of malignant disease, negative in 16 cases (59⅓ per cent.), and questionable in 2 cases (8⅓ per cent.). In non-malignant cases of various kinds, 15 (20 per cent.) gave a positive reaction, 55 (75 per cent.) gave a negative reaction, and 3 (15 per cent.) gave a doubtful reaction. He concludes that the test is only suggestive, and thinks it is rendered practically valueless as a diagnostic aid, because of the fact that there are undoubtedly present in the blood of many patients other lysins of unknown nature, which bring about hemolysis of varying degree.

The technique employed by Elsberg, Neuhof, and Geist consisted in the subcutaneous injection into the forearm of 5 minims of a 20 per cent. suspension (in normal salt solution) of washed human red corpuscles. These corpuscles were obtained from a normal healthy individual. They state that the reaction begins to appear as a rule, about five hours after the injection, gradually increasing in intensity until it has reached its height in six to eight hours. When fully developed the reaction appears as a somewhat irregular oval area measuring from 1 x 2 to 3 x 5 cm., with a well-defined margin. The margin is often surrounded by a whitish areola. The color varies from a brownish red to a maroon, with, rarely, a bluish tinge. The lesion is distinctly raised from the surrounding skin, slightly boggy on palpation, and often somewhat tender between the time of appearance of the reaction and its fading vary. When the lesion has disappeared there remains behind a flat yellowish or greenish discoloration, such as is left by any ecchymosis. Negative cases show either the point of needle puncture only or a small flat area of varying color; rarely the skin is raised but of normal color. Their work comprised 684 injections in 432 patients, and, in brief, an analysis of their cases showed a characteristic, easily recognizable reaction at the site of injection in 89.9 per cent. of cases suffering from carcinoma, and no reaction in 94.3 per cent. of cases from carcinoma.

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[6] Loc. cit.

[7] Loc. cit.

[8] Boston Med. and Surg. Jour., No. 4, clxv, 127.

At first we followed their technique, giving 21 injections to 21 patients; 15 of these patients, suffering from various medical diseases other than cancer, gave negative reactions.

One white patient of this series of 21, who had an adenocarcinoma of the rectum, showed a marked positive reaction.

One case of acute endocarditis with purpura, as one might expect, showed a strongly positive reaction.

The remaining 4 cases were colored patients, of whom 3 were cancerous. No reaction could be recognized in them, because of the pigmented skin. Negroes were not used in later observations.

One case with anacidity, on whom exploratory laparotomy was advised because of the suspicion of cancer of the stomach, gave a negative reaction. Subsequent operation disclosed gallstones and no carcinoma.

NORMAL ISOAGGLUTININS AND ISOHEMOLYSINS. At this juncture the communication of Moss,[9] "Studies on Isoagglutinins and Isohemolysins," suggested the possibility of a relation between the skin reaction described by Elsberg, Neuhof, and Geist, and the presence of normal isohemolysins. Were such the case, the value of the test from a specific diagnostic standpoint would be *nil*.

It seemed to us that the only confirmation of the skin reaction that was to have a real scientific value must include a determination of the grouping of the patients and an injection into each patient of red blood cells belonging to each of the four agglutinin groups. Thus a ready comparison could be made between the reaction *in vivo* and that in the test-tube.

Moss is of the opinion that every human being will fall into one of the following four groups, and that this grouping is established shortly after birth, and does not vary through life, in health, or in disease.

Group I	Serum agglutinates no corpuscles. Corpuscles agglutinated by serum of Groups II, III, IV.
Group II	Serum agglutinates corpuscles of Groups I and III. Corpuscles agglutinated by serum of Groups III and IV.
Group III	Serum agglutinates corpuscles of Groups I and II. Corpuscles agglutinated by serum of Groups II and IV.
Group IV	Serum agglutinates corpuscles of Groups I, II, and III. Corpuscles agglutinated by no serum.

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[9] Loc. cit.

Although he did not observe hemolysis as frequently or as consistently as agglutination, yet he believes that hemolysis never acts contrary to the laws of agglutination, as stated in the foregoing table.

Accordingly, if the reaction *in vivo* were the same as that in the test-tube, one would expect (from the above table) that patients belonging to Group I would give no reaction against any of the four different groups of corpuscles injected, because their serum agglutinates no corpuscles, and of course hemolyzes none.

Patients belonging to Group II might give a reaction with corpuscles from Groups I and III.

Patients belonging to Group III might give a reaction with corpuscles from Groups I and II.

Patients belonging to Group IV might give a reaction with corpuscles from Groups I, II, and III.

DETERMINATION OF AGGLUTIN GROUPS. Naturally, in order to test the above, it became necessary to obtain members of the four groups mentioned. Moss found that representatives of Groups II and IV were quite common, whereas Groups I and III were comparatively rare. In his report of a hundred group determinations he found the following percentages: Group I, 10 per cent.; Group II, 40 per cent.; Group III, 7 per cent.; Group IV, 43 per cent.

In our series, 45 individuals were examined before a Group I was found, so that we decided to extend these observations with the purpose of confirming Moss' findings. The results of determinations in 192 cases follow:

	Healthy.		Ill.		Total.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Group I	3	5	10	8	13	6.7
Group II . . .	22	34	42	33	64	33.3
Group III . . .	4	6	16	13	20	10.0
Group IV . . .	35	55	60	46	95	50.0

Within reasonable limits, then, our results compare very closely with those of Moss, as regards the relative frequency of the groups, with the exception that Group III is more common than Group I; likewise, it is interesting to note that with the exception of Group III the percentages vary but slightly between healthy and diseased individuals, and a larger series of cases would probably diminish this discrepancy.

It is perhaps worth recording that the agglutination reaction of the various groups differs, as regards the rapidity with which the reaction takes place. Group IV, for example, must possess serum of extraordinary power, for complete agglutination occurs within five minutes after mixing the serum and the corpuscles. Group II, on the other hand, frequently cannot be recognized for fifteen minutes to half an hour, and Group III requires still longer for positive identification. Group I agglutinates no corpuscles.

In determining the groups to which the patients belonged both the microscopic and macroscopic methods were employed.

TECHNIQUE OF THE SKIN REACTION. The technique employed by us in performing the skin test in the cases to be reported was as follows: On the day before the tests were to be made, 4 individuals were selected, 1 from each of the four groups, care being taken to exclude patients having syphilis or any other transmissible disease. Under aseptic conditions 15 c.c. of blood were removed from a vein of the forearm and immediately introduced into sodium citrate, to prevent clotting. It is important to wash out the syringe with sodium citrate before use, in order to prevent any hemolysis from water left in the syringe after boiling. The corpuscles thus obtained were centrifugalized, the supernatant fluid pipetted off, and the cells washed three times with normal salt solution. Strictly aseptic technique was observed throughout.

A 20 per cent. suspension of each set of corpuscles was then made and allowed to remain over night in the ice chest. They were then ready for injection, and were drawn up into sterile syringes previously washed out with normal salt solution.

The entire flexor surface of the forearm of the patient to be tested was rendered surgically clean. Five cubic centimeters of blood were taken from a vein of the patient's forearm with a needle and syringe, previously boiled and washed out thoroughly with sterile sodium citrate. The blood was introduced into a sterile tube, allowed to clot, and the clear serum removed with a capillary pipette, ½ c.c. of serum being placed in each of four test-tubes. Then ½ c.c. of a 5 per cent. suspension of Group I corpuscles was added to the serum in tube No. 1. One-half of a cubic centimeter of a 5 per cent. suspension of Group II corpuscles was added to the serum in tube No. II. Similar mixtures of the patient's serum and corpuscles were made with Groups III and IV. The tubes were shaken and allowed to remain in the thermostat for two hours at 36° C. Readings were then made for agglutination and hemolysis. The grouping was readily determined by noting the tubes in which agglutination had occured. Hemolysis was observed in various grades. Even slight traces were noted, in order to furnish data for comparison with the skin reaction.

After removing the 5 c.c. of blood from the forearm for the test-tube reaction ⅓ c.c. of the corpuscle suspension of each of the four groups prepared the day before was injected subcutaneously into the forearm at points about 5 cm. apart. The injection should be given under the skin and not into it. A small bulla at once appears when the injection is properly given, which soon subsides, leaving a pin-point abrasion where the needle entered. When the skin itself is injected discoloration may appear immediately and may cause confusion in interpreting the result. In selecting the site of injection, one should avoid superficial veins. It is advisable to give injections early in the day so that observation by daylight is possible. The corpuscles used were never more than twenty-four hours old.

Observations of patients were made four, six, and eight hours after injection. Our readings both of the skin reaction and of the test-tube controls were made independently by us, and our findings compared only after each series of experiments had been completed. In every case they were in entire accord.

Table I includes the diagnosis in each case, with the isohemolysin and isoagglutinin group to which each patient belongs. It then graphically compares, side by side, the reaction of the patient's serum upon the corpuscles of each group *in vivo* and *in vitro*, the former being the skin reaction and the latter the test-tube reaction. Thus we have the patient's serum acting on the four different groups of corpuscles in the body tissues and in the test-tube.

This table comprises 123 cases, 15 of which were examples of various types of carcinoma in which the diagnosis was verified by operation, autopsy, or microscopic examination; 1 unverified case of carcinoma; 3 cases of sarcoma; and 103 cases of normal individuals, and patients suffering from various ailments, including cardiopathies, pneumonia, gout, malaria, pellagra, amebic dysentery, dementia paralytica, nephropathies, cirrhosis of the liver, arthritides, hernia, idiocy, gangrene, morphinism, epilepsy, pernicious anemia, fractures, neurasthenia, syphilis, etc.

The results of this detailed report are compiled in Table II, which shows 60 per cent. positive reactions (against all four groups) in cases of carcinoma; 13 per cent. doubtful reactions; and 27 per cent. negative reactions. In cases other than malignant disease (103), 10 per cent. were positive; 2 per cent. doubtful; and 88 per cent. negative.

DISCUSSION OF THEORETICAL BASIS OF SKIN REACTION. We have been able to show conclusively in our series of cases that not infrequently a patient's serum possesses marked hemolytic power for one, two, or three kinds of corpuscles when tested outside the body in the test-tube, whereas the same serum acting against the same corpuscles *in vivo* produces no hemolysis whatever. As an instance of this phenomenon, we cite a case of pleurisy Group IV, which gave no reaction whatever in the body, but completely hemolyzed the corpuscles of Groups I, II, and III in the test-tube. There were 16 such examples in our series. This would seem to show that a reaction for carcinoma depending upon the test-tube hemolysis, as proposed by Crile, would be quite unreliable, since isohemolysis occurs frequently in normal individuals, as well as in persons with various non-malignant diseases.

TABLE I.—Result of Skin Reaction as Compared with Hemolysis in Vitro, Using Corpuscles from the Four Groups.

No.	Group.	Name.	Diagnosis	How made.	Corpuscles, Group I.		Corpuscles, Group II.		Corpuscles, Group III.		Corpuscles, Group IV.	
					Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.
1	..	Singer, H.	Adenocarcinoma, rectum	Operation	Positive	reaction.	Group of	corpuscles	used not	determined		
2	II	Golinsky, G.	Carcinoma, breast	Operation	+	0	+	0	+	0	+	0
3	II	Carroll, H.	Carcinoma, uterus	Operation	+	0	+	0	+	0	+	0
?4	I	——, C.	Sarcoma, arm	Operation	+	0	+	0	+	0	+	0
5	III	——, D.	Carcinoma, jaw	Operation	+?	+	+?	+	+?	0	+?	0
6	IV	Horwitz, B.	Carcinoma, breast (recurr.)	Operation	..	..	+	..	+			
7	I	Bay View Hosp.	Carcinoma, stomach	Autopsy	0	0	0	0	0	0	0	0
8	IV	Bay View Hosp.	Epithelioma, face	Operation	+	0	+	0	+	0	+	0
9	I	Bay View Hosp.	Epithelioma, head	Microscopic	0	0	0	0	0	0	0	0
10	III	Bay View Hosp.	Carcinomatosis	Autopsy	+?	+	+?	0	+?	0	+?	0
11	..	Matthews, G.	Carcinoma, breast	Operation	+	..	+	..	+	..	+	
12	..	Kimple, G.	Carcinoma, bladder	Operation	+	..	+	..	+	..	+	
13	IV	Nelson, D.	Carcinoma, rectum	Operation	0	0	0	0	0	0	0	0
14	IV	Ryan, H.	Carcinoma, cervix	Operation	+	+	+	+	+	+	+	0
15	..	——, G.	Carcinoma, breast	Operation	+	..	+	..	+	..	+	
16	..	Starkey, H.	Carcinoma, bladder	Microscopic	+	..	+	..	+	..	+	
*17	IV	2d test case 8	Epithelioma, face	Operation	0	0	0	0	0	0	0	0
18	II	Bay View Hosp.	Carcinoma, tongue	Microscopic	0	0	0	0	0	0	0	0
19	IV	Thomas, F.	Carcinoma, stomach	Clinical mass	0	+	0	+	0	0	0	0
*20	II	Summers, D.	Sarcoma, leg	Operation	0	0	0	0	0	0	0	0
*21	II	Hines, D.	Sarcoma, neck	Operation	0	0	0	0	0	0	0	0
22	II	Bluett, D.	Chronic appendicitis and gallstones	Operation	0	0	0	0	0	0	0	0

TABLE I.—(*Continued.*)

Group.	Diagnosis.	Corpuscles, Group I.		Corpuscles, Group II.		Corpuscles, Group III.		Corpuscles, Group IV.	
		Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis. in vitro.
IV	Normal individual	+	0	+	0	+	0	+	0
II	Normal individual	0	0	0	0	0	0	0	0
IV	Normal individual, tested three times	0	....	0	....	0	....	0	
II	Normal individual, tested two times	0	0	0	0	0	0	0	0
III	Hernia	0	0	0	+	0	0	0	0
IV	Hernia	0	0	0	+	0	+	0	0
II	Hernia	0	0	0	0	0	0	0	0
IV	Hernia	0	0	0	+	0	0	0	0
I	Hernia	0	0	0	0	0	0	0	0
IV	Hernia	0	0	0	0	0	0	0	0
I	Fracture	0	0	+?	0	0	0	0	0
IV	Fracture	0	+	0	+	0	+	0	0
	SPECIFIC INFECTIOUS DISEASES.								
IV	Pneumonia	0	0	0	0	0	0	0	0
I	Pneumonia	0	0	0	0	0	0	0	0
	Pneumonia	Negative	reaction.	Group of corpuscles used		not determined.			
	Pneumonia	Negative	reaction.	Group of corpuscles used		not determined.			
II	Influenza	0	0	0	0	0	0	0	0
I	Rheumatic fever	0	0	0	0	0	0	0	0
IV	Rheumatic fever	0	+	0	+	0	+	0	0
II	Malarial fever	0	0	0	0	0	0	0	0
IV	Malarial fever	0	0	0	0	0	0	0	0
	Malarial fever	Negative	reaction.						
III	Syphilis	0	0	0	0	0	0	0	0
IV	Syphilis	+	0	+	0	+	0	+	0
II	Syphilis	0	0	0	0	0	0	0	0
II	Syphilis	0	0	0	0	0	0	0	0
	Syphilis	Negative	reaction.						
I	Tabes dorsalis	0	0	0	0	0	0	0	0
	Spastic paralysis—luetic (?)	Negative	reaction.						
	Gonorrheal arthritis	Negative	reaction.						

TABLE I.—(*Continued.*)

Group.	Diagnosis.	Corpuscles, Group I.		Corpuscles, Group II		Corpuscles, Group III.		Corpuscles, Group IV	
		Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.	Skin reaction.	Hemolysis in vitro.
II	Tuberculosis, pulmonary	0	+	0	0	0	+	0	0
IV	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
IV	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
IV	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
II	Tuberculosis, pulmonary	0	0	0	0	0	0	0	0
	Tuberculosis, pulmonary	Negative	reaction.						
IV	Tuberculosis, pleural effusion	0	0	0	0	0	0	0	0
IV	Tuberculosis, fibrinous pleurisy	0	+	0	+	0	+	0	0
II	Tuberculosis, larynx	+?	+	+?	0	+?	+	+?	0
IV	Tuberculosis, osteomyelitis	+	0	+	0	+	0	+	0
	CONSTITUTIONAL DISEASES.								
II	Diabetes	0	0	+	0	+	0	0	0
II	Diabetes	+	0	+	0	+	0	+	0
IV	Diabetes	+	+	+	+	+	0	+	0
	....	0		0		0		0	
	Acute gout	Negative	reaction.						
III	Cardiac disease	0	0	0	0	0	0	0	0
IV	Cardiac disease	0	0	+	0	+	0	0	0
IV	Cardiac disease	0	0	0	0	0	0	0	0
IV	Cardiac disease	0	0	0	0	0	0	0	0
IV	Cardiac disease	0	+	0	0	0	+	0	0
IV	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease	0	0	0	0	0	0	0	0
II	Cardiac disease, tested twice	0	0	0	0	0	0	0	0
III	Cardiac disease	0	0	0	0	0	0	0	0
II	Endocarditis	0	0	0	0	0	0	0	0
IV	Endocarditis, purpura	0	0	0	0	0	0	0	0
	Endocarditis, purpura	Positive	reaction.						

MISCELLANEOUS DISEASES.

II	City Hospital, Bay View	0	0	0	0	0	0	0	0
III	City Hospital, Bay View	0	0	0	0	0	0	0	0
IV	City Hospital, Bay View	0	0	0	0	0	0	0	0
II	City Hospital, Bay View	0	0	0	0	+?	0	0	0
II	City Hospital, Bay View	0	0	0	0	0	0	0	0
II	City Hospital, Bay View	0	0	0	0	0	0	0	0
IV	City Hospital, Bay View	0	0	0	0	0	0	0	0
IV	High-grade idiot	0	0	0	0	0	0	0	0
IV	Neurasthenia	0	0	0	0	0	0	0	0
II	Infectious arthritis	0	0	0	0	0	0	0	0
IV	Infectious arthritis	0?	+	0?	+	0?	+	0?	0
II	Pernicious anemia	0	+	0	0	0	+	0	0
II	Osteomyelitis	+	0	+	0	+	0	+	0
IV	Goitre	0	+	0	0	0	0	0	0
II	Neuralgia, occipital	+	0	+	0	+	0	+	0
II	Chronic bronchitis	+	0	+	0	+	0	+	0
I	Chronic infectious arthritis	0	0	0	0	+?	0	0	0
III	Epilepsy	0	0	+	0	+	0	0	0
II	Morphinism	0	0	0	0	0	0	0	0
IV	Varicose ulcer	0	0	0	0	0	0	0	0
I	Gangrene, frostbite	0	0	0	0	0	0	0	0
IV	Myalgia	0	0	0	0	0	0	0	0
	Arteriosclerosis	+	0	+	+	0	+	0	+
	Gallstones	Negative	reaction.						
II	Hemiplegia	0	0	0	0	0	0	0	0
	Cerebral arteriosclerosis	Negative	reaction.						
III	Amebic dysentery	0	0	0	0	0	0	0	0
	Amebic dysentery	Negative	reaction.						
	Amebic dysentery	Negative	reaction.						
	Uncinariasis	Negative	reaction.						
II	Ulcer of the stomach	0	+	0	0	0	+	0	0
II	Pyloric stenosis	0	0	0	0	0	0	0	0
IV	Hyperacidity	+	+	+	+	+	0	+	0
IV	Enteroptosis	0	0	0	0	0	0	0	0
II	Cirrhosis of the liver	0	0	0	0	0	0	0	0

SURGICAL DISEASES.

	Goldberg, D.	0	....	0	....	0	....	0	
	Bartusak, D.	0	....	0	....	0	....	0	
	Robier, D.	0	....	0	....	0	....	0	
	Templeman, D.	0	....	0	....	0	....	0	
	Mallow, D.	0	....	0	....	0	....	0	
	Frits, D.	0	....	0	....	0	....	0	
	Carpenter, D.	0	....	0	....	0	....	0	
	Hege, D.	0	....	0	....	0	....	0	

TABLE II.

	Positive.	Per cent.	Negative.	Per cent.	Doubtful.	Per cent.	Total.
Verified cancer cases	9	60	4	27	2	13	15
Doubtful cancer cases	..	..	1	..	..	..	1
Verified sarcoma cases	1	33⅓	2	66⅔	..	..	3
Non-malignant cases	10	10	91	88	2	2	103
Cancer case	..	..	..	..	..	..	1
Once positive (No. 8)							
Once negative (No. 17)							
Grand total							123

In Case No. 20 the test was made after amputation.

Vice versa, we have had cases showing marked positive reactions in the body whose sera showed absolutely no hemolytic power against the same corpuscles when tested *in vitro*. As an instance of this reverse phenomenon, we cite a case of sarcoma of the arm which gave a strong positive reaction against each of the four groups of corpuscles *in vivo*, but no hemolysis against the same corpuscles in the test-tube. Elsberg, Neuhof, and Geist[10] explain the reaction as follows:

"If normal blood cells are injected under the skin of a patient whose serum is hemolytic, fresh quantities of hemolysin would be continually brought to the cells by the circulating blood and lymph, and, therefore, even if the amount of hemolysin in the blood of the patient was very small, the injected cells might, nevertheless, be hemolyzed. Every organic substance which was liberated by the destruction of the injected red cells would enter the tissues and there have its effect. The hemoglobin and other substances which had been set free might cause a local change in the tissues at the site of the injection. If blood cells are injected under the skin of a normal individual, they are broken up and carried off by the body cells and fluids; the condition of affairs under the skin of a patient whose blood serum contains free hemolysins would be an entirely different one because a different process was taking place."

Elsberg, Neuhof, and Geist's hypothesis that the reaction may be due to a larger quantity of hemolysin containing serum constantly bathing the injected cells does not explain all the facts, since some sera show strong hemolytic properties *in vitro* and none *in vivo*. So it seems justifiable to assume that there may be two hemolysins or hemolytic processes, one of which is met with in the body in some cases, especially carcinoma; the other of which occurs in test-tube reactions when the serum of normal or of diseased persons is allowed to act on red blood cells. Our small series of about 400 injections and 400 test-tube controls shows no relation existing between these two types.

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[10] Loc. cit.

Accordingly, our expectation that the normal isohemolysis would account for an appreciable number of the positive skin reactions has not been realized. In none of our cases showing an outspoken skin reaction, was there any relation existing between the intensity of the reaction and the isoagglutinin or hemolysin grouping of the corpuscles.

However, the utilization of the four groups of corpuscles for injection has revealed the significant fact that it is not a matter of indifference as to the type of corpuscles selected for the test. Our series of cases shows several instances in which the reaction was positive about one or two of the corpuscle groups and negative at the site of injection of the others. Such cases were considered negative. Only those were called positive in which all four types of corpuscles were affected. So it is conceivable that the injection of simply one type of corpuscles, the group of which is unknown, might lead to an erroneous deduction. In spite of this, however, there appears to be one group of corpuscles, namely, Group IV, which might be utilized for the reaction with reasonable reliability. It will be remembered that the corpuscles of Group IV are neither agglutinated nor hemolyzed by any sera *in vitro*. In our entire series of 124 cases, in which the four types of corpuscles were injected subcutaneously, not a single instance was observed in which the corpuscles of Group IV gave a positive reaction without the corpuscles of Groups I, II, and III also showing a positive reaction.

Accordingly, from the above results, if a positive reaction were obtained about the site of injection, of corpuscles from Group IV, it would be *ipso facto* evidence that corpuscles from Groups I, II, and III would likewise have been hemolyzed. On the other hand, if a negative reaction were the result of such an injection the test would be considered negative, even if corpuscles from Groups I, II, or III would have given a positive reaction.

It is not justifiable, however, to reach a definite conclusion on this point from the study of so few cases. The action of Group IV corpuscles should be observed in an extended series of cases where all four types are injected. If this point is substantiated, then the injection of Group IV corpuscles alone will prove sufficient for the reaction.

Perhaps it should be noted that our decision to consider a skin reaction positive only when all four groups of corpuscles are hemolyzed is an arbitrary one, since further study may show that the different groups have different powers of resistance to the sera of cancer patients.

After reviewing this work we feel reasonably confident that our main object has been accomplished; namely, placing the carcinoma skin reaction on a conservative scientific basis. The actual clinical value of the test is by no means determined, but we are of the opinion that it can be determined now with accuracy. Many problems in connection with this reaction, bearing upon its aid in the diagnosis of malignant disease are now open for solution.

1. Whether a positive reaction can be secured in early cases of malignant disease, where the clinical diagnosis is quite doubtful, thus permitting early operative interference.

2. Whether the reaction can be utilized as an index of cure after complete radical operations; and how soon the reaction disappears after operation, provided it has been positive before.

3. Whether the reappearance of a positive reaction two or three years after operation would be indicative of recurrence.

These and many other problems are of great interest, but can be determined only after large series of cases have been tested with repeated injections over a long period of time. But we feel that as a result of this work, such problems can now be readily solved and the true diagnostic value of this reaction judged precisely.

CONCLUSIONS. 1. The test is certainly not specific for carcinoma. We have found it positive in somewhat more than half of patients suffering from cancer (60 per cent.) and negative in a large majority of patients showing other forms of disease (about 89 per cent.) It may prove to be another help in the diagnosis of cancer, and its value is sufficient to warrant the application of the test and study in large series of cases.

2. Apparently no connection exists between a positive skin reaction and hemolysis in the test-tube. The test-tube method is of questionable value.

3. The grouping to which the corpuscles employed for injection belong is not a matter of indifference but one of considerable importance.

4. We are not prepared to speak as to the special value of the reaction in differentiating early carcinoma and borderline tumors, or as to its absence in advanced cases.

5. A positive reaction is of much greater significance than a negative one. If the reaction is positive, the patient very probably suffers from cancer; if, however, it be negative, cancer cannot be excluded.

We desire to express our appreciation of the constant interest and advice of Dr. Moss, under whom this work was completed, and to acknowledge further the kindness of Drs. Barker, Halsted, and Finney in allowing us the privilege of their cases; to thank Drs. Sladen, Remsen, and Cullen and other members of the resident hospital staff of the Johns Hopkins Hospital for assisting us in obtaining suitable cases; likewise Dr. Boggs for placing at our disposal the patients at the City Hospital, Bay View.